Study shows benefits of anti-clotting medications reduced by common heartburn drugs

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The anti-clotting action of the medication clopidogrel (Plavix) can be compromised by common drugs for the treatment of heartburn and ulcers resulting in a roughly 50% increase in the combined risk of hospitalization for heart attack, stroke and other serious cardiovascular illnesses, according to a new study presented today at the Society for Cardiovascular Angiography and Interventions (SCAI) 32nd Annual Scientific Sessions. The study specifically focused on the effects of proton pump inhibitors (PPI) omeprazole (Prilosec), esomeprazole (Nexium), pantoprazole (Protonix), and lansoprazole (Prevacid), which together accounted for about 96% of PPI use in the study.

Patients who receive a drug-eluting stent benefit from taking anti-clotting medications, including thienopyradines (such as clopidogrel or ticlopidine) and aspirin, for at least one year following the procedure. Doctors often also prescribe PPIs to patients taking clopidogrel because of pre-existing stomach disease or to reduce the risk of common side effects such as nausea and gastroesophageal reflux (heartburn). Before clopidogrel can exert its anti-clotting effects, it must be converted from its inactive, pro-drug form to an active drug by enzymes in the liver. PPIs—the sixth most commonly prescribed drug class in the U.S.—can interfere with those liver enzymes, according to the study.

"Given the large number of patients who undergo coronary stent procedures each year, and the recommended and wide use of clopidogrel

following this procedure, our findings have implications for many thousands of patients across the United States," said Eric J. Stanek, PharmD, senior director of research, personalized medicine research and development, Medco Health Solutions, Franklin Lakes, NJ, and the study's principal investigator. "Clopidogrel should continue to be taken as prescribed, and the need for PPI therapy should be carefully evaluated to ensure that it is prescribed only when clearly indicated."

For the study, researchers analyzed integrated data on pharmacy and medical claims from more than 10 million patients, including 16,690 patients taking clopidogrel for a full year following coronary stenting. Of these, 41% also took a PPI, on average, for more than nine months of the year. Over that 12-month period when patients took clopidogrel, investigators evaluated the risk of hospitalization for major adverse cardiovascular events (MACE), which they defined as a combination of heart attack, unstable angina, stroke or temporary stroke-like symptoms, repeat coronary procedures, or cardiovascular death.

The overall MACE risk was 51% higher among patients taking any PPI. The findings were equally concerning when the effects of individual PPIs were analyzed. Omeprazole correlated with a 39% increased risk of MACE, esomeprazole to a 57% increased risk, pantoprazole to a 61% increased risk and lansoprazole to a 39% increased risk. All of the associations were highly statistically significant. Overall, the incidence of hospitalization for upper gastrointestinal bleeding was only 1.1% among patients taking a PPI and 0.07% among those not taking a PPI.

Additional research is needed to determine whether newer, less widely used PPIs such as rabeprazole (Aciphex) and dexlansoprazole (Kapidex) are also associated with increased cardiovascular risk in patients taking clopidogrel. Researchers are also interested in examining how genetic variations in the liver enzymes that activate clopidogrel might alter the impact of PPIs on clopidogrel effectiveness, the potential influence of

the timing of PPI administration, the effect of alternate dosing of clopidogrel, and the comparative effectiveness of other anti-clotting medications.

Source: Society for Cardiovascular Angiography and Interventions

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